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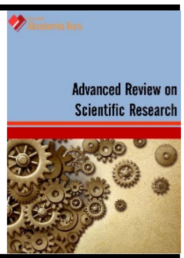

A review on quantitative ultrasound of fast and slow waves

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ABSTRACT

Offering inexpensive, widely available and safe method to evaluate the bone condition as a prevention step to predict bone fracture which caused by Osteoporosis disease makes ultrasound becomes an alternative method beside X-ray based bone densitometry. Conventional quantitative ultrasound (QUS) applies the analysis of attenuation and velocity to estimate bone health with several measurement techniques which analyzes different types of ultrasound waves and bones. However, most of the QUS results still does not match the accuracy of the Dual X-ray absorptiometry due to the interaction of ultrasound and bone microstructure are not fully exploited. The Biot's theory has predicted that, porous medium like a cancellous bone supporting two types of longitudinal wave known as fast and slow wave which depends on the type of medium travelled. Both experiment and simulation were conducted to investigate the correlation of fast and slow waves individually with a variety of cancellous bone condition. Some of the analysis methods are based on conventional QUS methods. The fast and slow wave relates more to the microstructure of the cancellous bone compared to overall waves. In addition, overall waves had been proven to consist of fast and slow wave and can be separated using Bayesian methods. Overall waves also found to suffer artifact such as phase cancellation and negative dispersion that could cause confusion in analyzing the parameters of ultrasound wave with bone structure. In vivo application based on fast and slow wave analysis is able to produce results based on mass density which can be compared directly and have high correlation with X-ray based bone densitometry. The recent backscattered simulation result indicates that, fast and slow waves can be reflected inside the cancellous bone might offer a new method to evaluate bone especially in crucial skeletal parts.

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1. Introduction

Ultrasound is a cyclic sound pressure with frequencies greater than 20 kHz, the limit of human hearing [1, 2]. In medical, diagnostic, ultrasound frequency used ranges from 1 to 20 MHz [1, 3].

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There are several modalities of the ultrasound medical application such as A-mode, B-mode, M-mode and Doppler imaging where each modality has their own specific uses [4]. Ultrasound technology is known as one of the non-destructive technique (NDT) to monitor the condition and the flaws in medium such as composite material [5-6]. From the clinical aspect, the ultrasound possesses invaluable interest due to widely available, low cost, non-ionizing radiation, portable, short examination time, and capability of the real time image display [3, 7]. Ultrasound technology was introduced for bone related purpose taking place since 1950 where the ultrasound application was used to monitor fracture healing at the tibia (shin bone) [8]. Ultrasound wave also can be used to determine the geometrical outcome of double co-planar edge cracks on the stress intensity factor in the human femur bone. The results of these findings can be used to suggest appropriate implants to minimize the effects of stress at the bone, thereby speeding up the time taken by the bone to recover from the fracture [9].

Fundamentally, bone can be characterized into cortical (compact) and cancellous (also known as trabecular or spongy) bone as shown in Figure 1 [10]. The transition region of bone volume decreases gradually from cortical site and trabecular side, thus difficult to decide a clear borderline between those types of bones [11]. Previous research suggested that, only 70% to 80% of the variance of bone strength is accounted for by bone density [12] another percent is from microstructural of bone as well as the bone architecture which is the arrangement of the bone material in space [4]. Cancellous bone is described as rod-alike or plate like trabeculae filled with viscous marrow is in the pore space [13, 14]. In addition, cancellous bone has a high degree of porosity, anisotropy, and inhomogeneity [15-18] and because of that, the interaction between ultrasound waves is complex [19] and porosity of cancellous bone changes according to its position within the bone [20]. Porosity level of cancellous bone is around 50% to 90% [13, 21] and volume fraction (BV/TV) less than 70%. Effect of decreased bone density is stronger for cancellous bone than for dense cortical bone because the cancellous bone is metabolically active [22]. Cortical bone represented by a shell of complex shape, a fragment of which can be roughly approximated by a plate or a fragment of a tube [23]. In microstructure level, cancellous bone consists of a cylindrical structure called trabeculae whereas cortical bone, consist of osteon or Haverstan system [21]. Moreover, cortical bones contain numerous mechanical, microstructural, and macro-structural properties [23].

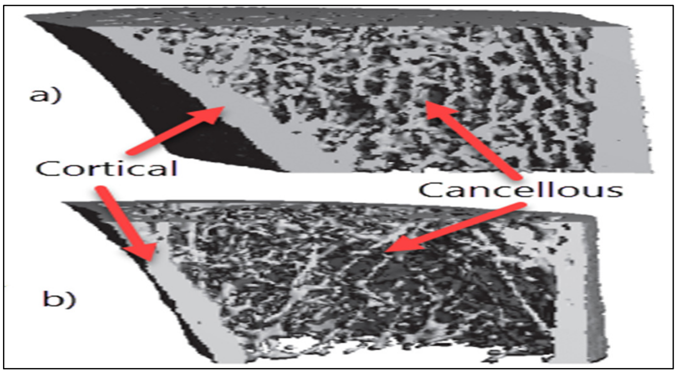

Fig. 1. Cross section of bone consists of cortical and cancellous bone; a) is normal bone and, b) bone due to osteoporosis [29]

As the human age increase, the quality of the overall human bone will decrease. The difference is that the rate of bone quality decreases depending on diet, lifestyle, and diseases related to the bone. Research suggested bone losses in old age or cortical thickness decreasing and increase of porosity in cortical and cancellous bone [14, 24]. This condition will increase fracture risk. Besides, there is several specific clinical population of fracture risk such as postmenopausal women suffer osteoporosis, thoroughbred racehorse in training and astronauts who worked for months on the space station [25-26]. Osteoporosis disease is famously known worldwide as metabolic bone disease [27] which affects bone quality and increases fracture risk among elderly people especially postmenopausal women. The manifestation of fracture risk increase because Osteoporosis causes low bone density and microstructural deterioration as shown in Figure 1 [17, 19, 23, 28]. It is also causing cortical thinning and cancellous bone perforation [18]. Typical fracture risk occurs at hip, spine and wrist of the sufferers. Among osteoporotic fracture sites, the hip fracture is riskier, as it has a high death rate of 15-30% [10].

The primary method for diagnosing osteoporosis and associated fracture risk relies on bone densitometry to measure bone mass [30]. Based on bone mass measurement, World Health Organization (WHO) has set-up a variable which known as T-score to determine Osteoporosis level among patients. In addition, the use of bone mass is based on the well-established thesis that bone strength is strongly related to the amount of bone material present and that a stronger bone in a given individual is associated generally with a lower fracture risk [30]. The density of the mineral phase of the bone corresponds to bone mass density (BMD) [10]. This density can be measured with Dual X-ray Absorptiometry (DXA) and X-ray quantitative computed tomography (QCT) [30, 31]. DXA is the standard diagnostic method for osteoporosis assessment which is considered as the 'gold' standard to BMD at the hip, spine, and forearm with measurement unit of g cm-2 [30, 31]. However, QCT is capable of performing a three-dimensional (3-D) scan of bone and enabling differentiation between cortical and cancellous bone densities with clearly with unit g cm-3. Nevertheless, both are not widely available due to its high expense, inconvenience, and the reluctance among patients concerning X-ray exposure, mainly in young adults and children [30].

2. Quantitative Ultrasound

The quantitative ultrasound (QUS) is introduced in the field of osteoporosis and followed by several publications of the studies in 1980 [3, 32]. Several bone sites have been measured in vivo application such as calcaneal (heel bone), finger phalanges, tibia, proximal femur, and radius [3]. The concept of QUS is transmitting of ultrasound wave through bone to measure density, elasticity and structure of the bone. Bone tissue either soft or hard tissue is characterized in terms of ultrasonic velocity and attenuation [30]. The main contributions of attenuation of bone are absorbing and scattering due to its internal material [33-35]. Moreover, there are several techniques to measure ultrasound wave correlation on bone such as through-transmission (TT), axial transmission (AT), and Pulse echo (PE) as shown in Figure 2. Between these three techniques, only TT technique has been researched fast and slow wave thoroughly in experiment and simulation.

2.1 Through-Transmission (TT)

Through-transmission (TT) technique is the earliest technique used to measure the quality of the heel bone. The basic concept of TT measurement technique is with pair of ultrasound transducer which acts as a transmitter and the other one acting as a receiver which is placed facing with each other [3, 25]. The transmitter emit ultrasound wave which passes through test sample and received at the receiver. A TT technique in vivo can be divided into two methods which are dry contact method and substitution method [25]. For the dry contact method, transducer is in contact with subject heel and uses coupling gel as coupling agent while in substitution method, the subject heel is submerged in a water-bath [1]. The transmitter transducer is typically fed by pulse generator with very short signal spike or single sinusoidal wave.

Fig. 2. Measurement techniques; a) TT technique, b) AT technique, and c) PE technique

Conventional QUS method to analyze attenuation using this technique begins with the reference wave obtained by transmitting and received an ultrasound wave in water only. Then, the transducer transmits ultrasound again with water and test sample in between the transducers. The received wave then compared with reference wave in a certain frequency range where the analysis is known as broadband ultrasound attenuation (BUA) and if the estimation includes sample thickness, it is called as normalized BUA (nBUA).

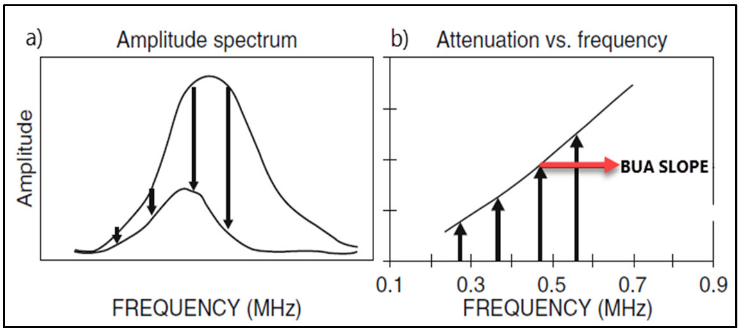

Fig. 3. BUA; a) Amplitude spectrum comparison between water and bone, b) Graph attenuation versus frequency [3]

The comparison is based on the power spectrum of each wave which has been obtained using Discrete Fast Fourier transform (DFFT). The typical frequency ranging was from 0.2 to 0.6 MHz and the data was expressed as the increase in ultrasonic attenuation with frequency (dB/MHz) for BUA while nBUA is (dB/MHz/cm) [25, 36]. Then, the slope of attenuation versus frequency was calculated to obtained BUA or nBUA value as shown in Figure 3. Previous research shows that, both values were related to density and structure of cancellous bone [25, 36]. For ultrasound speed, the term of speed of sound (SOS) is used and expressed in (m/s). SOS measurement capability is used to estimate density and elasticity of the bone [25, 37]. However, because there is no consensus on a standardized protocol for velocity determinations in bone, the comparison or pooling of measurements obtained from different devices is particularly difficult [3]. To obtain SOS, time of flight (TOF) of the ultrasound wave is measured. The TOF is the elapsed time from transmission of an ultrasound pulse to the detection of a received pulse [10, 38]. Hence, SOS can be calculated using TOF information which has been acquired. Comparison ultrasound with X-ray based densitometry measurements, both the SOS and BUA showed a clear relationship with the BMD measurement especially on the heel bone [28].

3. Fast and Slow Wave

Behaviors of ultrasound wave parameters are depending on the medium which the wave passes through. Velocity and attenuation of ultrasound wave propagation through a solid medium differ with propagation through viscous medium. Regarding of bone, cancellous bone can be considered as a porous medium which consist of inhomogeneous solid trabecular and bone marrow in the pore (viscous medium) [15-18]. In other words, there are two types of material and structure inside cancellous bone, solid and viscous liquid. Hence, when a single mode ultrasound wave propagates through cancellous bone, it might produce two modes of ultrasound waves propagate inside the cancellous bone due to its internal structure and materials. This phenomenon has been predicted by Biot's theory which adopting the theory of geophysical testing of porous rock [19]. The Biot's theory predicts that two longitudinal waves, which were indicated as "waves of the first and second kind", are able to propagate through a fluid saturated porous elastic solid [39].

The first kind is known as fast wave while the second kind is slow wave. It was considered that the experimentally observed fast and slow waves in cancellous bone might be related to the two waves predicted in the Biot's theory. Then, the Biot's theory has been used to predict the properties of both wave propagations using cancellous bone by using the Biot's model for simulation-based investigation [39]. The Biot's model is a reference model for wave propagation in porous media based on homogenization theory, particularly because it has shown to predict effectively the velocities of two longitudinal waves in various porous media from sintered glass, cortical bone and cancellous bone [16].

The early Biot's model has several drawbacks such as only limited to low frequency only due to the ultrasound wavelengths are of the equal order of magnitude as the dimension of the trabeculae [16]. In addition, Biot's model doesn't predict the scattering effect. Thus, to overcome the problems modified Biot's model is introduced. The modified model has included the parameter of scattering and shows a good agreement between theoretical and experimental, in term of speed and also attenuation. By solving the inverse problem, modified Biot's model is able to give an estimation of bone structural parameters [39]. However, both Biot's model required many parameters that are challenging to measure in the situation of cancellous bone, especially in vivo [16, 27].

The experimental observation of the fast and slow longitudinal waves propagating in cancellous bone was first reported by Hosokawa and Otani in 1997 [39]. The fast wave is characterized as in-phase and slow wave is out-of-phase wave between fluid and solid [13]. In other words, fast wave related to solid trabecular while the slow wave is related to bone marrow (viscous medium). Parameter of fast and slow wave is able to provide the speed and amplitude that have correlated with bone parameters such as porosity, bone volume fraction (density), temperature (bone marrow), viscoelasticity and trabecular distribution [22, 40-44]. Hence, recovering the ultrasound properties of the individual fast and slow wave, as an alternative of the overall waves, may lead to improvement of bone quality assessment [19].

Despite cancellous bone was proven to support propagation of fast and slow waves, several considerations must be done to ensure clear observation of fast and slow wave especially in time domain. The first consideration relates to the transducers properties used for transmitting and receiving the ultrasound pulse wave. A very short pulse wave is required for observing the two waves separately. However, the observation of both waves cannot essentially be improved by increasing frequency since the attenuation of the fast wave is high at frequencies over 1 MHz [39]. The second consideration is depending on the direction of wave propagation relative to the anatomical orientation of cancellous bone. The cancellous bone had a strong acoustic anisotropy and that the observed waveform propagating through bone changed with the propagation direction to the trabecular orientation as the degree of anisotropy (DA) increases [39].

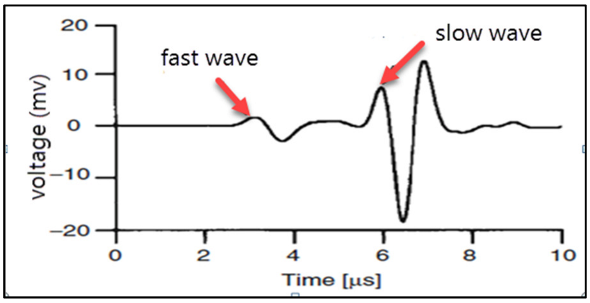

Fig. 4. Observable fast and slow wave in time domain [39]

Nevertheless, there are some situations which can cause fast and slow waves overlap with each other and complicate the analyzing process. Propagation of ultrasound wave is known to depend on DA where the existence of fast and slow wave has been observed significantly dependent on the insonification angle relative to the predominant trabecular alignment. In other words, parallel with trabecular alignment [13, 18, 19, 22, 30, 39, 44-45]. Several laboratories reported that, when the propagation of the ultrasound wave path is perpendicular to the trabecular alignment, fast and slow wave will be overlap each other [30, 39, 44, 46]. Therefore, a number of methods to separate fast and slow waves emerged to resolve the issue such as Bayesian methods [44-45].

Due to different reaction in terms of amplitude and velocity between fast and slow waves against cancellous bone microstructure, each wave has their own characteristics and can be used to identify fast and slow wave observed from overall waves. The frequency content of the spectrum within each wave is different. Fast wave has low frequency spectral content compared to slow wave which has high frequency spectral content [43]. The amplitude of the slow wave usually bigger compared to slow wave. In terms of time arrival, fast wave arrives first, followed by slow waves as shown in Figure 4.

4. Methodology

Based on conventional QUS analysis methods, fast and slow waves were analyzed separately to increase accuracy of the bone quality estimation due to their unique responds with the microstructure of cancellous bone. In addition, the measurement technique used was through-transmission (TT) technique since it is more appropriately used to measure ultrasound parameters of cancellous bone. Most early studies limited with experiment-based investigation to study the correlation of ultrasound wave with bone microstructure. Through time, most of the research was based on a simulation method, especially Finite Different Time Domain (FDTD). Simulation method provides opportunities for researchers to investigate any new possibility and idea to fill the research gap before set up any experiment. Simulation method also much cheaper compared to experiment set up and some real time signalling problem such as noise can be easily eliminated [40, 47].

4.1 Experimental Specimens and Simulation Models

There are various types of test sample for investigation of fast and slow wave. The most typical is the real cancellous bone. Bone specimens used are usually from bovine bone and human bone [43-44]. Femoral and calcaneal bone are examples of bone specimen which taken from human donor with various ages and conditions [43-44]. Besides, investigation of bone marrow was conducted using bone specimens from the femur and tibia [42]. In most experiment, the bone specimen was cut into simpler shapes such as a cube or cuboid with dimension in the range of millimetre. Any remaining of bone marrow was removed with pressurize water. The bone specimen was cleaned using some sort of chemical solution such as trichloroethylene for several hours [43]. Then, air bubble from bone specimen was removed by placing the bone specimen in the measurement cell in a vacuum vessel [39, 43]. Furthermore, some researcher develops bone phantom to facilitate the process of investigation of bone, especially complex structure of cancellous bone [17-18]. Some of the phantom were based on 3D print from Micro-CT scanned real horse bone [17] and made off from water saturated aluminium foam with an open network of interconnected ligaments [18].

Moreover, numerical synthesize models were used for simulation-based investigation. The common models were Micro-CT scanned bone models. The model was developed by using (2-D) or (3-D) scan of animal and human bone using Micro-CT and implement into the FDTD environment [15, 20, 40, 41, 45, 48]. Some more examples of numerical synthesize model are such as Biot's model, Independent Scattering Approximation (ISA), multilayer fluid-solid model, and scattering model [16, 19]. These model's mechanical parameters can be altered to suit with the objective of the research. However, these models usually used as a start of the research and the result obtained often compared with experiment result for evaluation process either suitable to be used as surrogate of cancellous bone [15, 19, 48].

4.2 Ultrasound Apparatus for Experiment

The experiment usually conducted inside a modified water tank. The water tank was filled with water or degassed water (which CO_2 or O_2 contents were removed) to act as a medium to ease ultrasound propagation [39]. Based on TT measurement technique, ultrasound transducers used were paired immersion transducer type. One of the transducers connected to pulse generator that feed with single sinusoidal or very short spike signal [39] with frequency ranging 0.1 to 1 MHz. The other one connected to Oscilloscope and Analog-to-Digital (A/D) converter to record overall received waveform with a sampling frequency in Megahertz range. The recorded waveform then analyzes using appropriate software.

4.3 Fast and Slow Wave Analysis

The first thing to do before computing any parameters, fast and slow wave must be identified from the overall recorded waveform. For situation which fast and slow wave clearly separated as observed in time domain, the calculation of parameters such as attenuation and velocity can be done directly. However, some situations required to implement noise cancellation, for example unable to observe fast wave amplitude due to small in amplitude [18]. Hence, coded excitation method was used to enhance received waveform. Example of coded excitation method is Golay code [49-50]. In the case of fast and slow wave overlapping each other due to measurement take place not at the trabecular alignment, both waves need to separate using wave separation method such as Bayesian method [44-45]. In addition, Bayesian method separate fast and slow wave by estimates three parameters of fast and slow wave such as velocity, amplitude and frequency [44]. After each wave was obtained, further analysis can be carried out.

To investigate attenuation coefficient for each of fast and slow waves, analysis method used was based on nBUA but some researcher name it as frequency dependent ultrasound attenuation (FDUA) as to avoid confusion from nBUA [43]. The FDUA analyze attenuation coefficient of fast and slow waves separately by creating two sections of time windows based on bandwidth of interest [43]. The two sections of time windows were used to "capture" each fast and slow wave as well as acquiring amplitude spectrum each wave using DFFT. The power spectrum of each wave was compared with a power spectrum of reference wave which was obtained using the same technique as conventional QUS (refer TT measurement technique). The step was repeated for every ultrasound wave frequency ranging from 0.2 to 0.6 MHz and slope of the attenuation versus frequency was acquired. This analysis method was done for every bone specimen with various parameters in order to study the effect of bone microstructure against the attenuation coefficient each fast and slow wave.

The attenuation coefficient at each frequency within the bandwidth of interest in frequency domain, in units of dB/cm, can be determined by performing a log-spectral subtraction technique of the form [30, 44]

$$\alpha(f) = \frac{10\log(|\tilde{V}w(f)|^2 - 10\log(|\tilde{V}s(f)|^2)}{d} \quad (1)$$

where $|\tilde{V}w(f)|^2$ and $|\tilde{V}s(f)|^2$ are the power spectra of the reference and bone specimen wave respectively. For time domain calculation, attenuation calculation given by

$$\alpha(t) = \frac{20\log(\frac{V_n}{V_{n+1}})}{\Delta d} \quad (2)$$

where V_n and V_{n+1} are the amplitudes of the first arriving peaks in the received waveforms. The indices *n* and *n+1* correspond to successive sample thicknesses differing by Δd = 1 mm [30]. Besides, based on observation in the time domain, fast and slow waves exhibit different frequency value. To prove the hypothesis, DFFT was applies to the overall recorded waveform slope of the graph was observed based on bandwidth of interest which has been set previously [43].

In term of velocity analysis, there are two types of velocity calculated from the longitudinal ultrasound wave which are group velocity and phase velocity. Group velocity resembles physically to the velocity at which information or energy is carried alongside the direction of propagation while phase velocity relates to the propagation velocity of a given phase that is of a single frequency component of a periodic wave [2]. Group velocity can be estimated from measurement of TOF or calculation, and its value usually lower than the phase velocity [51]. Group velocities calculation given by

$$v_{group} = \frac{h}{-\Delta t + \frac{h}{V_{water}}} \quad (3)$$

where Δt is the delay time between the traveling times of the reference points of the signals, and h is the sample thickness [18]. For phase velocity calculation is given by

$$v_{phase}(\omega) = v_{water}\left[1 - \frac{v_{water}}{d}\frac{\Delta\emptyset(\omega)}{\omega}\right]^{-1} \tag{4}$$

where V_{water} is the velocity in water, d is the sample thickness, $\Delta\varphi(\omega)$ is the difference in unwrapped phase between the sample and reference signals, and ω is angular frequency. Despite phase velocity can be calculated in this direct approach, using it as a reliable indicator of bone quality is troubled because the physics of ultrasonic waves in cancellous bone that relate to dispersion remains incompletely understood. One example is the apparent conflict between the dispersion predicted by the causality-imposed Kramers-Kronig relations and that observed experimentally [46, 51-52].

5. Results and Discussions

Based on information about cancellous bone losses, a number of investigations have already been conducted by manipulating bones structure parameter such as porosity, density, trabecular homogeneity, temperature (bone marrow) and others [22, 40-43, 53]. These studies were to observed parameters each of fast and slow waves against a variety of cancellous bone, internal structure as well as result in comparison with overall waves in both experiment and simulation methods.

Overall waves are basically comprised of two modes (fast and slow wave) longitudinal wave overlapping each other during propagation through cancellous bone [44, 45]. The theory is consistent with the result obtained in an attempt to separate fast and slow wave using Bayesian method [44]. The amplitude of the overall waves is higher compared with individual fast and slow wave [44]. In addition, result from phase velocity measurement for eight bone specimens with various porosity levels shows that, the phase velocity of overall waves always located between the fast and slow wave phase velocities [44]. Both results show that, a combination of fast and slow wave amplitude and velocity will produce overall waves. Not only that, overall waves nBUA (FDUA) analysis was consistently larger than the nBUA value obtained from each fast and slow waves.

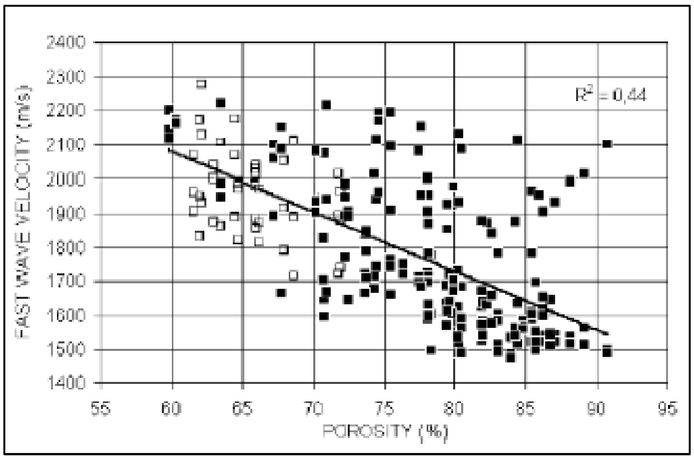

Fig. 5. Fast wave velocity as function to various levels of porosity human cancellous bone (black) and bovine cancellous bone (white) [43]

This is due to interference between these two wave modes is unintentionally being perceived as a true signal loss occurring within the whole sample [30, 44]. Regarding of research on frequency spectral content for each fast and slow waves, the graph of attenuation versus frequency for overall recorded waveform was plotted by Cardoso et al. and demonstrate that the slope of fast wave is much steeper with ranged of frequency from approximately 0.5 MHz to 1 MHz whereas slow wave is much more moderate with frequency ranged from 1 MHz to 2.5 MHz.The result shows that, fast wave have low frequency spectral component, whereas slow wave have high frequency spectral component [43]. Moreover, Cardoso et al. also investigate relation between fast and slow wave parameters with human and bovine bone porosity. Velocity measurement shows that, the fast wave velocity for both specimens ranged from 1500 to 2300 m/s. For bovine specimens, velocity is much higher compared to human specimen. In general, velocity of fast wave decrease as porosity increases. Regression value is computed ($R^2 = 0.44$, $p < 10^{-3}$) with moderate but significant correlation to porosity [43] as shown in Figure 5.

Compared to slow wave, velocity of slow wave is analyzed based on two types of velocity, which are frequency dependent velocity and frequency independent velocity as shown in Figure 6. Frequency dependent velocity values increased with porosity (1150–1500 m/s) whereas frequency independent velocity propagates with an almost constant velocity (1450–1490 m/s) [43]. Both groups reached the same velocity value at high porosity however for below 80% porosity, they were clearly identified. Both parameters were significantly correlated for the first slow wave group only ($R^2 = 0.26$, $p < 10^{-3}$) [43]. The phenomenon shows that the fast and slow waves (frequency dependent) correspond to the waves propagate mainly in the solid bone and pore part of the cancellous bone respectively [16, 43, 53]. However, for frequency independent velocity of slow wave was close to the velocity of sound in the fluid alone. This wave does not affected by porosity as well as the orientation of the specimen which could relate either a direct propagation in the fluid through large pores of the solid trabecular or an artifact caused by wave propagation at the boundary of the specimen [43].

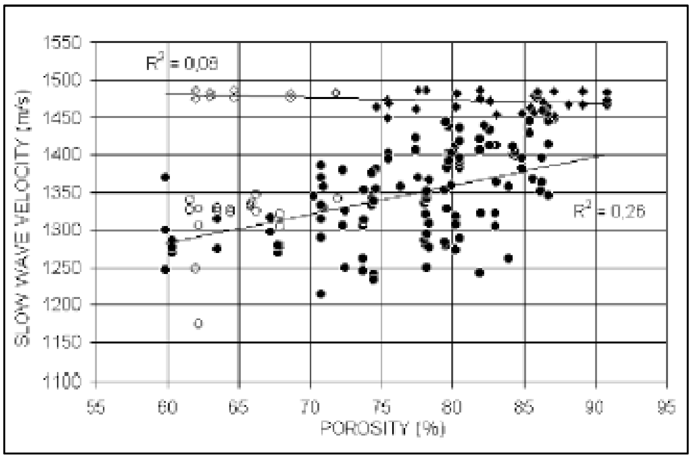

Fig. 6. Slow wave velocities versus porosity. Black is human cancellous bone and white is bovine cancellous bone. Two types of velocity, circles indicate frequency dependent velocity and diamond is frequency independent velocity [43]

For FDUA measurement which based on Figure 7, the fast wave FDUA exhibits a parabolic behaviour (R2 = 0.41, p < 10-3) with a maximum around 75% of porosity (140 dB/cm MHz), whereas for the slow wave FDUA (in the 15–40 dB/cm MHz range), increase slightly with porosity (R2 = 0.15, p < 10-2) [43]. Similarly to velocity behaviour, both fast and slow wave FDUAs reached the same value for high porosities.

The behaviour may cause by the existence of two waves traveling together. The resulting overall attenuation is a combination of both wave attenuation spectrums. The most porous specimen which is high porosity, the lower attenuation of slow wave covered the attenuation of fast wave. The calculation of fast wave attenuation for high porosity might be combination of fast and slow wave attenuation thus explain the reason fast and slow wave FDUAs reach the same value for the highest porosities [43].

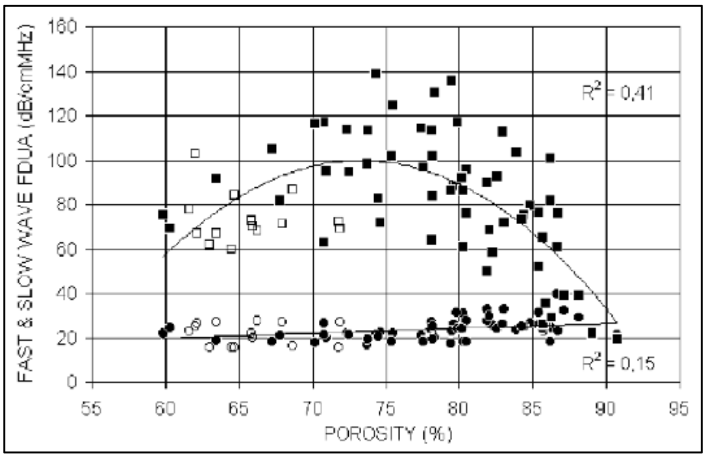

Fig. 7. Fast and slow wave attenuation value (FDUA) with increasing porosity for human cancellous bone (black) and bovine cancellous bone (white) [43]

Besides porosity, degree of anisotropy (DA) also affects fast and slow wave propagation in cancellous bone. Previous FDTD simulation with (2-D) model of bovine bone [15] and recent experiment towards (3-D) 1:1 scale of trabecular bone phantom from horse bone [17] manipulated two directions of propagation which are parallel and perpendicular to trabecular alignment. The received waveform obtained by Mézière et al. indicate, with the propagation direction parallel to trabecular alignment, fast and slow wave was observed separately while perpendicular direction, only one wave was observed as shown in Figure 8 as the test toward bone phantom. It shows a good agreement with the results of others who concluded that, observation of these two modes significantly dependent on the insonification angle relative to the predominant trabecular alignment [13, 18, 19, 22, 30, 44-45].

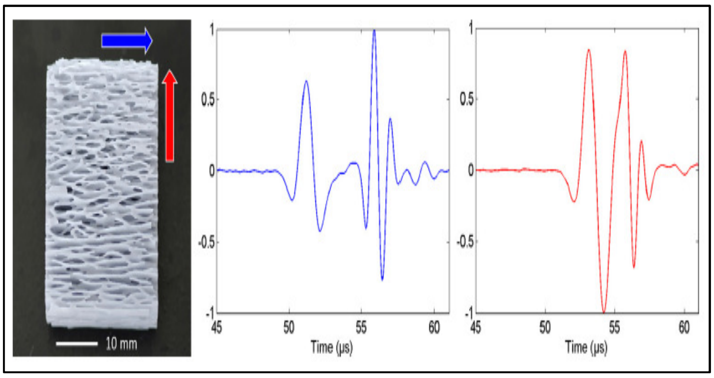

Fig. 8. Two behaviour of received wave based on propagation direction of the ultrasound, blue waveform parallel and red waveform perpendicular towards trabecular alignment [17]

Furthermore, density or bone volume fraction (BV/TV) also studied using real cancellous bone [22] and bone phantom based on water saturated aluminium foam [18]. Zhang *et al*. [18] setting the parameter for the density of the phantom as an Aluminium Volume Fraction (AVF) and the study are carried out together with pores per inch (PPI) to observed parameters of fast and slow waves. Due to the amplitude of fast wave is too small to observed, the results focus on the frequency range where the slow waves dominated [18]. The phase velocities test result shows that, all phase velocities are lower than the acoustic velocity in water, which is consistent with the group velocity measurements and thus confirms the dominance of slow wave propagation in the samples. The phase velocity decreases with increasing AVF. Furthermore, the majority of the samples exhibit positive dispersion (phase velocity increasing with frequency) which good agreement with other result [26, 30, 51]. However, not for 5% AVF with 15 PPI, which show slightly negative dispersion [18]. The possible causes for negative dispersion are the scattering effects including multiple scattering and the interference between the fast and slow waves same as reported by other laboratories [18, 30, 46, 51] even though the fast waves in that case have extremely small amplitudes. The claim was supported by other laboratories report, which, when fast and slow wave analyzed separately, no negative dispersion was observed [26, 30, 46].

Regarding of attenuation measurement, generally attenuation increases with PPI; for each PPI, attenuation increases with an AVF which indicate that slow wave correlate with pore part of the cancellous bone [16, 43, 53] whereas the attenuation of the 20 PPI samples with frequency is less obvious and exhibits a non-increasing attenuation level within the main frequency range. The 20 PPI samples have more pores which are smaller and comparable to the dominant wavelength and as a consequence, a more number of scattering interfaces. This enhances the scattering processes among ligaments within the samples, giving rise to the low intensity noise signals affecting the interest signals. More volume averaging due to a broad pulse is expected when the ultrasound beam passes through the samples and thus generates a smoother transmitted signal. Both the scattering and volume averaging are perhaps the dominant processes contributing to the non-increasing attenuation behaviour of the 20 PPI samples [18].

Furthermore, Otani and Shimoi conducting experiment with real cancellous bones to determine correlation of BV/TV of the cancellous bone with fast and slow waves were observed in term of wave amplitude and speed [22]. The graph of BV/TV versus speed and amplitude each fast and slow wave shows that, a strong positive correlation between fast wave speed and amplitude increase when BV/TV increases and a clear negative correlation for the slow wave which amplitude and velocity decrease with increases of BV/TV [22]. However, speed of slow wave shows low correlation with BV/TV compared with the speed of fast wave, hence can be assumed, fast wave correlate more with density and solid part of the cancellous bone compared to slow wave [22].

Nevertheless, Hosokawa manipulate porosity distribution to study relation with fast and slow waves [20]. Using FDTD simulation, microstructure of the cancellous bone model was altered using the erosion procedure [54]. It is found that, both wave amplitude (fast and slow wave) increased when porosity distribution was low and when the trabecular structure was more uniforms whereas the speed of the fast wave increase when porosity distribution was high and long trabecular element were present. Hence, the propagation properties of the fast wave are related mainly to the solid part of cancellous bone [20].

There are also researches to study the effect of changes in the bone marrow with fast and slow wave. Among parameter used are temperature and presence of viscoelasticity of bone marrow [41-42]. Increasing environment temperature (water tank) caused the speed of slow wave decrease, but slightly increased in amplitude, but no significant effect of fast wave thus proving that slow waves propagate mainly through bone marrow [42]. In terms of viscoelasticity presence, amplitude of slow wave increase when viscoelasticity in bone increase. As for fast wave, amplitude is decreased when viscoelasticity in bone increase [41]. Again, the result has good agreement with the claims which state that, fast and slow wave propagate mainly to solid and pore part of cancellous bone respectively [16, 22, 43, 53].

Behaviour of fast and slow waves propagate with various cancellous bone thickness was studied using simulation methods [30]. The fast and slow wave was separated using Bayesian method and attenuation coefficient both in time and frequency domains was computed. Not only that, the result of attenuation coefficient from individual fast and slow wave was compared with overall waves. In time domain, both overall and individual fast and slow wave attenuation coefficient decrease as thickness of bone sample increase. The explanation for the occurrence is because estimating the attenuation from the time-domain amplitude of a broadband pulse which is 1 MHz frequency was used for the current system. Usually, the attenuation coefficient for both fast and slow waves increases with frequency in the certain ranges.

Table 1
Summary of result and discussion of past researches

No.	Type of research	Wave mode	Analysis	Manipulated variables	References
1.	In vitro experiment (heel bone)	Single & two modes	1. Bayesian wave separation method 2. Comparison single and two modes (nBUA and phase velocity)	Various microstructure of the bone specimen	[44]
2.	FDTD simulation (3D bovine bone)	Two modes	Amplitude and speed of ultrasound waveform	Porosity distribution	[20]
3.	FDTD simulation (Numerical synthesize model)	Single & two modes	Numerical model comparison based on velocity and attenuation between Biot, Wood and ISA model.	1. Acoustic anisotropy 2. Solid fraction	[16]
4.	FDTD simulation (3D bovine bone)	Two modes	Amplitude of ultrasound waveform	Viscosity presence	[41]
5.	FDTD simulation (2D bone model)	Two modes	Comparison Biot model, 2D model and experiment (waveform observation)	Acoustic anisotropy	[15]
6.	Experiment (bone phantom)	Single & two modes	Frequency dependent attenuation, phase velocity & The root-mean-squared error (RMSE)	AVF = BV/TV	[18]
7.	In vitro experiment (bovine bone)	Single & two modes	1. Waveform plot in time and frequency domain 2. Frequency dependent attenuation	Thickness	[30]
8.	Experiment	Two modes	1. Comparison actual bone and bone phantom. 2. Waveform observation in time domain	Acoustic anisotropy	[17]
9.	Experiment & simulation	Two modes	Comparison experiment and simulation based on Frequency dependent attenuation, SOS, and waveform amplitude.	1. BV/TV 2. Porosity	[22]
10.	In vitro experiment (distal femur and proximal tibia)	Single& two modes	1. Velocity and frequency dependent attenuation. 2. Waveform observation in time domain	Temperature	[42]
11.	In vitro experiment (human and bovine bone)	Single & two modes	1. FDUA 2. Velocity 3. Each fast and slow wave characteristics analysis	Porosity	[43]

As a result, during initial propagation, the higher frequency components of the broadband wave are reduced more quickly than the lower frequency waves, hence resulting in a wave exhibiting correspondingly more of the lower frequency components which are attenuated less with distance than the higher frequencies, resulting in a perceived attenuation coefficient that appears to decrease with distance [30]. Moreover, the frequency domain investigation result shows that, overall waves exhibit an increase in attenuation from thickness 0.8 to about 1.0 cm and decrease moderately until sample thickness of 1.4 cm [30].

In addition, the values of attenuation coefficient are negative below sample thicknesses of 0.8 cm due to interference between the fast and slow waves [30]. The attenuation coefficient remains constant for each fast and slow waves for all various sample's thickness [30]. The frequency domain analysis method does affect for the broadband nature of the result. However, applying this method to the overall waveform still produces which appear as an attenuation coefficient that depends on the thickness of the sample which looks like to be a result of interference between the fast and slow waves being perceived as attenuation [30]. Thus, analyze each of fast and slow wave can avoid such artifacts. Another artifact might occur due to interference of fast and slow wave such as phase cancellation [30, 51]. Table 1 summarizes the overall result and discussion section.

6. Applications and Future of Fast and Slow waves

In vivo application based on fast and slow wave have already been introduced and known as new QUS [39]. The measurement takes place at the wrist using TT technique and the system has been commercialized by the name of LD-100 [39, 55-57]. Compared with conventional QUS, the new QUS analyze both fast and slow wave parameters which conventional QUS not considered [39, 55-56]. The system diagnoses done twice with the first scan are to determine the appropriate wrist area which contains more bones [39]. The second scan will measure ultrasound wave parameters including new variables such as cancellous bone density, elasticity and cortical thickness, which acquired using a PE technique [39, 55-56]. In addition, cancellous bone density and cortical thickness measurement from new QUS compared with X-ray based densitometry, a highly significant correlation was found between both systems [55]. Hence, ultrasound-based bone diagnostic can be as powerful as X-ray based densitometry with inexpensive, non-radiating and widely available [5].

Besides TT measurement technique which limited with several skeletal parts [3, 58], another recent research pursue measurement of fast and slow wave in overall backscattered waves might prove exist and could be distinguished from overall backscattered wave from a deeper bone depth when propagate in cancellous bone. The discovery was acquired from a study on backscattered wave via FDTD simulation [40]. The study also indicates that, the amplitude of fast and slow backscattered waves were more closely correlated with the bone porosity than the amplitude of the overall backscattered waves [40].

7. Conclusion

In conclusion, ultrasound technologies continue to research and applied in the medical field despite the existences of other technologies such as X-ray based technologies. The precision of QUS analysis was comparable with X-ray based bone densitometry shows a promising to be an alternative method to evaluate the quality of the bone. Although, discovery of fast and slow waves as predict by Biot theory might changes in how the ultrasound wave really interacts with cancellous bone due to its complex nature. The investigation of these two modes longitudinal waves has carried out in experiment and simulation. A number of studies of fast and slow waves using through-transmission technique and analysis based on conventional QUS have revealed that fast and slow waves are more related to variations of microstructure of bone compared to overall waves. In addition, the overall waves result also might affected by the artifacts such as negative dispersion and phase cancelation which can cause misinterpretations of information regarding of bone conditions. Hence, it is important to analyze fast and slow wave separately given that a method to separate these waves from overall waves also available. In vivo application based on these two modes ultrasound waves also showing a more precise plus new additional variables which allow a direct comparison with X-ray based bone densitometry. However, it does not stop the research in the exploitation of fast and slow waves because backscattered wave also proven supporting propagation of these modes which probably overcome the issue to evaluate bone quality of the spine and hip bone.

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